HHS Public Access

Author manuscript

Thromb Res. Author manuscript; available in PMC 2016 September 01.

Published in final edited form as:

Thromb Res. 2015 September ; 136(3): 535–541. doi:10.1016/j.thromres.2015.06.036.

Characteristics and Risk Factors of Cancer Associated Venous Thromboembolism☆

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Abstract

Introduction—The objective of this study was to examine the differences in commonly associated characteristics and risk factors of venous thromboembolism (VTE) between patients with and without cancer in a VTE population.

Materials and Methods—Uniform data were collected for patients with a diagnosis of VTE obtaining care at CDC funded Thrombosis Network Centers. Patient characteristics and risk factors were compared in VTE patients with and without cancer. Logistic regression was used to calculate the unadjusted and adjusted odds ratios (ORs) and 95% confidence intervals (CIs) to assess patient characteristics and thrombotic risk factors more frequently identified among VTE patients with cancer compared to those without cancer.

Results—Between August 2003 and April 2011, 3,115 adult patients with a diagnosis of VTE including 189 (6.1%) patients with active cancer participated in the multi-site thrombosis registry. VTE patients with cancer had a higher prevalence of PE and DVT in unusual sites compared to those without cancer. Thrombophilia was more common among VTE patients without cancer than those with cancer (25.1% vs 10.6%, $p < 0.001$). In adjusted analysis, age group ≥ 45 years (OR

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Conflict of Interest

None

=5.20, 95% CI, 3.30, 8.18), surgery (OR =1.86, 95% CI, 1.19, 2.91), and hypertension (OR =1.66, 95% CI, 1.15, 2.40) were the VTE risk factors more commonly found among VTE patients with cancer.

Conclusion—The study identified several thrombotic risk factors more likely to be found with cancer associated VTE, which may help to characterize at risk cancer patients and to develop prevention and management strategies in this population.

Keywords

Cancer; Malignancy; Venous Thromboembolism; Pulmonary Embolism; Deep Vein Thrombosis; Thrombophilia

1. Introduction

Venous thromboembolism (VTE) including deep vein thrombosis (DVT) and pulmonary embolism (PE) is a major public health problem with an annual incidence rate in the United States of 1–2 per 1000 adults [1]. VTE is a leading cause of death in cancer patients [2] and cancer patients have a substantially higher risk of death if they have a concurrent diagnosis of VTE [3].

Cancer is found in approximately 20% of patients with VTE [4] and patients with cancer have an approximately 4–7 fold increased risk of developing VTE compared to controls [5]. A population based study using inpatient discharge diagnoses from 1979–1999 found a 2% occurrence of VTE among patients with cancer which was twice the incidence in patients without malignancies [6].

The occurrence of VTE is a multicausal process that involves both genetic and acquired risk factors and/or an interaction between them [7]. Studies have demonstrated that hereditary and acquired risk factors, patient characteristics as well as triggering events contribute to the thrombotic risk [7–10] but the magnitude of effect of each factor may vary in the presence of other risk factors. Malignancy is associated with activation of the coagulation cascade. This prothrombotic state is further exacerbated by anti-cancer therapy including surgery, chemotherapy, radiotherapy and hormone therapy [11–13]. However, the role played by known hereditary and acquired factors and the interaction between these thrombotic risk factors in the development of VTE may not be the same in patients with cancer as in patients without cancer.

Several studies have examined the association of cancer with VTE and the role of hereditary and acquired risk factors in the development of VTE in cancer patients [3,6,13–18]. However, there are limited data for VTE patients with cancer compared to VTE patients without cancer [19,20] and the clinical characteristics and thrombotic risk factors in these patients are not fully known. A better understanding of differences in thrombotic risk factors in these patients may help to identify the most appropriate preventive and management approaches for patients with cancer. The objective of this study was to examine the distribution of clinical characteristics and thrombotic risk factors in VTE patients with cancer compared to VTE patients without cancer seen as outpatients in US Thrombosis and Hemostasis Network Centers.

2. Material and Methods

The study was conducted at Centers for Disease Control and Prevention (CDC) funded Thrombosis and Hemostasis Research and Prevention Network Centers. Patients obtaining care at these centers were approached for participation in the Networks' patient registry regardless of the reason for their center visit. Most of these patients were referred to centers in an outpatient setting for evaluation and management of thrombotic disease. After obtaining informed consent, a standardized data collection form was completed by centers' staff for initial and all subsequent visits for each consenting patient. Institutional Review Board approval was obtained at each of the network centers and the CDC annually.

Uniform data were collected for the patient registry from August 2003 to April 2011. Demographic and clinical characteristics, VTE characteristics, status of cancer with type and site of cancer, status of chemotherapy and radiotherapy, history of concurrent medical conditions, surgical procedures, trauma, family history of thrombophilia and VTE, laboratory and radiologic testing and treatments prescribed by the center were obtained for each patient. For female patients, obstetric history and information about use of hormonal contraceptives or hormone replacement therapy was additionally obtained. These data were entered into a secure web-based registry housed in CDC's Division of Blood Disorders. Only de-identified information, with an assigned number for study identification was submitted to CDC.

For this study, data obtained from multi-site patient registry on patients 18 years and older diagnosed with VTE were used. A diagnosis of VTE was made in the presence of a history of deep vein thrombosis (DVT) and/or pulmonary embolism (PE) and confirmed by radiographic imaging including ultrasound, ventilation perfusion scan (VQ scan), CT and/or MRI. All patients either with a history of VTE within 12 months of cancer diagnosis or with VTE occurring in the presence of active cancer were identified. Dates of diagnosis of cancer and diagnosis of VTE were used to define the temporal relationship of VTE with the diagnosis of cancer.

For the analyses, age at the time of enrollment was categorized as < 45 and ≥ 45 years. Data on race was based on self-report as White, Black or "Other" (non-white and non-black) and ethnicity was categorized as Hispanic or non-Hispanic. Smoking was defined as self-reported cigarette smoking at the time of any visit during the study period. Body mass index (BMI) was calculated from weight (kg) and height (m) measured (BMI = weight (kg)/height (m^2)) at enrollment and three categories of BMI were defined as < 18.5, 18.5 to 25 and > 25 kg/m^2.

The location of the DVT was identified in the database as arm or leg DVT, or thrombosis of abdominal veins or veins at other sites. Recurrent VTE was identified as the presence of a history of more than one episode of either DVT or PE at least one month apart. Idiopathic VTE was defined as DVT and/or PE in the absence of surgery, trauma, hospitalization, prolonged immobilization, pregnancy, or hormonal contraceptive or hormonal therapy use within 3 months of the VTE. For the purpose of this analysis, malignancy was not included

in the definition of secondary VTE as we wished to estimate the prevalence of “idiopathic” VTE among cancer patients.

A history of medical comorbidities (including diabetes mellitus, hypertension, hyperlipidemia, chronic liver and kidney disease and autoimmune disease) was obtained. Surgery, trauma or catheter-related VTE was defined as having the condition within three months prior to the VTE event. For female patients, VTE associated with hormone use was defined as the use of oral contraceptives or hormone replacement therapy within 3 months prior to the VTE.

The presence of thrombophilia was defined as a documented diagnosis of a hereditary or acquired thrombophilia (factor V Leiden mutation, prothrombin gene mutation, protein C, protein S, and antithrombin deficiencies, and antiphospholipid antibody syndrome). In most cases, thrombophilia was either diagnosed or confirmed by laboratory testing performed at the network centers. However, this testing was not necessary for entry in the CDC registry. Antiphospholipid antibody syndrome was diagnosed using international consensus criteria [14]. The presence of a self-reported family history was defined as a history of VTE in the family.

Patients with either a history of VTE within 12 months of cancer diagnosis or concurrent with active cancer were defined as patients with cancer or equivalently as having cancer-associated VTE; the remaining patients were defined as patients with VTE without cancer. To compare differences in the mean age and BMI of patients with and without cancer, student’s t-test was performed. Chi-square test was used to compare the frequencies of other patient characteristics between the two groups and in the case of small expected cell sizes (<5) Fisher’s exact p-values were reported. A p-value ≤ 0.05 was considered statistically significant for the analyses. Logistic regression analysis was used to calculate the unadjusted and adjusted odds ratios (ORs) and 95% confidence intervals (CIs). For adjusted analysis, race, Hispanic ethnicity, sex, BMI, smoking and other risk factors that met the $p \leq 0.05$ significance level were included in the model. Finally, the data were stratified by sex to evaluate male and female VTE patients separately. The data were analyzed using SAS statistical package (Version 9.2) (SAS Institute, Cary, NC).

3. Results

There were 3,115 adult patients with a diagnosis of VTE enrolled in the multi-site thrombosis registry between August 2003 and April 2011. Of these patients with VTE, we identified 189 (6.1%) patients with cancer and 2,806 patients without cancer. The characteristics of the patients with and without cancer are shown in Table 1. Patients with cancer were older at enrollment and at the time of first VTE event compared to patients without cancer; about 84% of patients with cancer were 45 years or older at the time of enrollment compared to 51% of patients without cancer. The distributions of race and sex were similar for patients with and without cancer. The mean BMI and prevalence of BMI $\geq$ 25 kg/m^2 at enrollment were higher in patients without cancer compared to patients with cancer. About 11% of patients without cancer and 6% with cancer reported smoking.

Post-surgical VTE was more common in patients with cancer (14.8% vs 9.3%, $p < 0.01$) compared to patients without cancer. However, there were no significant differences in trauma-associated VTE, recurrent episodes of VTE, idiopathic VTE and a family history of VTE between patients with and without cancer. Among female patients, use of hormone replacement therapy was higher in patients with cancer (6.3% vs 1.9%, $p = 0.009$) and use of hormonal contraceptives was higher in patients without cancer (12% vs 2.7%, $p = 0.003$).

Hypertension and hyperlipidemia were more common in VTE patients with cancer than in those without cancer (37.6% vs 19.1%, $p < 0.001$ and 16.9% vs 11.8%, $p = 0.03$) respectively, but the distribution of other comorbid medical conditions including diabetes mellitus, chronic liver and renal disease and autoimmune disease was similar in patients with and without cancer.

Thrombophilia was more common among patients without cancer than among patients with cancer (25.1% vs 10.6%, $p < 0.001$) (Table 2). This difference was largely due to factor V Leiden mutation which was found to be more common among patients without cancer than VTE patients with cancer (12.0% vs 5.3%; $p = 0.005$) (Table 3). Antiphospholipid antibody syndrome was also significantly higher among patients without cancer than those with cancer (7.6% vs 2.1%, $p = 0.005$). There were no significant differences in other thrombophilic risk factors.

The distribution of PE and DVT and location of DVT in patients with and without cancer are shown in Table 3. There was a higher proportion of PE among patients with cancer compared to VTE patients without cancer but the difference was not statistically significant. Venous thrombosis of the superior vena cava, inferior vena cava and thrombosis of the veins of the neck (14.8% vs 9.8%, $p = 0.03$) were more common in patients with cancer than those without cancer. Catheter-associated VTE was also more common in patients with cancer (4.8% vs 1.9%, $p = 0.02$). However, none of the patients with cancer had venous thrombosis of the brain unlike patients without cancer (0 vs 2.8%, $p = 0.009$).

The most common type of cancer among the cancer-associated VTE group was gynecological cancer followed by gastrointestinal tract, breast, hematological, genitourinary and lung cancer (Table 4). Brain and central nervous system cancer and head and neck cancer were less common. Twenty two percent (42/189) of the patients with cancer received chemotherapy and/or radiation therapy within 12 months of VTE. In addition, DVT was more common in patients with breast and brain cancer whereas PE ± DVT was more common in patients with skin, lung and genitourinary malignancies. The distribution of DVT and PE ± DVT by cancer type is shown in the Fig. 1.

Catheter-associated VTE was more common in patients with cancer than patients without cancer (4.8% vs 1.9%; $p < 0.01$) and 22% of patients with cancer and 15% of patients without cancer had catheter-associated thrombosis of the neck ($p = 0.57$). History of venous thromboembolism was also not significantly different between patients with and without cancer (7.3% vs 6.0%; $p = 0.17$).

Both male and female patients with cancer were older at enrollment and at the time of first VTE compared to patients without cancer. Among males (84.4% vs 64.6%; $p = 0.0004$) and

among females (83.0% vs 42.6%; p <0.0001) patients with cancer were more frequently in age group ≥ 45 years than those without cancer. Among males, a BMI ≥ 25 kg/m^2 (84.8% vs 72.5%; p = 0.007) was more common in patients without cancer compared to patients with cancer whereas surgery within three months of VTE diagnosis was more common in patients with cancer than those without cancer (18.2% vs 9.5%; p = 0.02). Among females, hypertension (43.8% vs 17.2%; p < 0.001), hyperlipidemia (15.2% vs 9.5%; p = 0.05) and diabetes (11.6% vs 6.4%; p = 0.03) were more prevalent in patients with cancer than those without cancer. Thrombophilia was more common in patients without cancer than in those with cancer in both males (22.1% vs 6.5%, p = 0.001) and females (26.9% vs 13.4%; p = 0.002). This was primarily due to factor V Leiden mutation (13.1% vs 6.3%; p = 0.04) and antiphospholipid syndrome (8.2% vs 1.8%; p = 0.01) in female patients and factor V Leiden mutation (10.3% vs 3.9%; p = 0.07) in male patients (data not shown).

In adjusted analysis, age group ≥ 45 years, surgery, hypertension remained more frequent among patients with cancer compared to those without cancer (Table 5). When stratified by sex, after adjusting for demographic and other risk factors, age group ≥ 45 was more common among the cancer group for both females and males. For females, hypertension and for males, surgery were also positively associated in patients with cancer compared to those without cancer (Table 6).

4. Discussion

The differences in characteristics and presence of thrombotic risk factors in patients with cancer compared to patients without an associated cancer diagnosis in a population of VTE patients have not been appreciated until now. This study identified 6.1% cancer-associated VTE in an outpatient VTE population and several differences in the presence of known VTE risk factors between patients with and without cancer in this population. Patients with cancer were older at the time of diagnosis of first VTE than patients without cancer. Thrombophilia and higher BMI were more common in patients without cancer. After adjusting for demographic and other risk factors commonly associated with VTE, age group ≥ 45 years, a history of major surgery and hypertension within 3 months of a diagnosis of VTE were more prevalent among patients with cancer. When stratified by sex, age group ≥ 45 years for both females and males, hypertension for females and surgery for males within 3 months of diagnosis of VTE were more frequently found among the patients with cancer than those without cancer.

Previous studies have reported risk factors of VTE in the general population [1,4,7–10,21–29] as well as in cancer patients [5,6,13–18, 30–37] but differences in the frequencies of risk factors have not been well described for patients with cancer compared to non cancer patients in a VTE population in an outpatient setting. A recent study in the United Kingdom [19] used registry data to examine demographics and characteristics of cancer-associated VTE in an outpatient VTE population. In our study, we evaluated demographics as well as both hereditary and acquired risk factors for cancer associated VTE in an outpatient VTE population. Another recent multicenter study reported three month mortality rate and clinical predictors in VTE patients with cancer from an ongoing thrombosis registry in a racially homogeneous population [20].

Paneesha et al. [19] found 13.6% of cancer cases among VTE patients which was much higher than 6.1% identified in our study. This difference could be explained by a much older VTE cohort in their study where mean age for cancer and non cancer cases were 66.4 ± 12.7 vs 58.8 ± 18.7 years (p value < 0.001) respectively, compared to 57.1 ± 14.7 vs 46.1 ± 15.5 years; p value < 0.0001 in our VTE population. It may also be possible that the VTE population seen at the participating centers in the UK Registry may be different from the VTE population seen at our Thrombosis Centers. They reported cancer associated VTE earlier in life for females than for males peaking in the sixth (21.4% vs 11.3%, p value <0.001) and seventh decades of life (21.7% vs 18%, p value =0.036) for females [19]. In our study, age was found to be a risk factor in patients with cancer associated VTE after adjusting for other confounding variables and although we found that females were younger than males at the time of cancer associated VTE, the difference in age was not statistically significant (50.5 ± 16.8 vs 54.8 ± 15.8, p value =0.08).

Gussoni et al. [20] reported 17.1% of cancer cases among VTE patients in an older and a racially homogeneous VTE cohort. The mean age for patients with cancer and those without cancer were 65 ± 18 vs 67 ± 13 years (p value < 0.001) respectively. There was also no significant difference between the history of VTE in patients with and without cancer in our study in contrast to the findings of the RIETE registry which reported prior VTE to be more common in patients with cancer than those without cancer [20].

There was an increased risk of secondary VTE reported in a study investigating the association of smoking with VTE [38] but data are limited for the risk of VTE with smoking in cancer patients. Our data showed a higher prevalence of smoking at the time of any visit in non cancer patients even in cases of secondary VTE. Our finding may be due to the fact that smoking was defined only as smoking during the study period and prior smoking history was not considered.

In our VTE cohort, about one third of patients with cancer and one quarter of patients without cancer had BMI < 25 kg/m^2 and although not statistically significant, BMI < 18.5 kg/m^2 was more frequent among patients with cancer. We repeated the analyses with obesity defined as BMI ≥ 30 kg/m^2 but the adjusted ORs did not show any significant change. A meta-analysis evaluating association between cardiovascular risk factors and VTE, reported an association between obesity and VTE (OR =2.33, 95% CI = 1.68, 3.24) [22]. Obesity was also one of the comorbidities associated with VTE in a cohort of hospitalized cancer patients (OR =1.56, 95% CI = 1.14, 2.15) [36]. However, the distribution of other categories of BMI has never been examined in VTE patients with cancer.

Preexisting medical comorbidities play an important role in the progression and treatment of VTE in the general population and in cancer patients medical comorbidities impact survival, the clinical course of the disease, and treatment choices [30]. We found hypertension to be more frequent in the patients with cancer even after adjusting for age, body mass index and other risk factors. However, when stratified by sex, the finding held for the female patients only. Hypertension has been reported as a risk factor for VTE in previous studies [21,22]. In a cohort of female nurses, hypertension was associated with an increased risk of PE with a relative risk of 1.9 (95% CI, 1.2, 2.8) even after adjusting for body mass index [21]. In a

meta-analysis, the risk of VTE was higher, OR = 1.51 (95% CI, 1.23, 1.85) in patients with hypertension compared to control subjects [22] and hypertension was one of the comorbidities identified as a risk factor of VTE among hospitalized cancer patients in a population-based study [37].

VTE has been found to be a common complication after major surgery in population based studies [23–25]. The occurrence of VTE after surgical procedures may be even higher in patients with cancer. Studies have shown that patients with cancer had higher incidence of VTE after various surgical procedures [25,39,40]. In our cohort of VTE patients, we found that surgery within three months of VTE was more common with cancer-associated VTE after adjusting for confounding variables. However, when stratified by sex, this applied to male patients only.

We did not find a significant difference in the frequency of recurrence in patients with cancer compared to patients without cancer. This is inconsistent with the findings of several other studies [33–35]. Using Medicare claims dataset, Levitan et al. [33] demonstrated that patients with concurrent DVT/PE and malignancy had a more than threefold higher risk of recurrent thromboembolic disease than patients with DVT/PE without malignancy. Prandoni et al. [34] reported a hazard ratio of 3.2 (95% CI, 1.9, 5.4) for recurrence of thromboembolism in cancer patients. This lack of association in our study may be explained by its cross-sectional design with unstructured follow up visits resulting in limited follow-up time for some patients including patients with cancer who may have died. In addition, since our study was conducted at Thrombosis and Hemostasis Centers there may be more patients with recurrent VTE overall than found in other studies.

There are limited data for the association of hereditary thrombophilia with VTE in cancer patients [5,41]. In a case control study with VTE patients as cases and their partners as controls, Blom et al. [5] reported that with a factor V Leiden mutation, the odds ratio was 12.1 (95% CI, 1.6, 88.1) for those with cancer and OR was 3.3 (95% CI, 2.6, 4.1) for those without cancer. However, in a cohort of cancer patients, Otterson [41] did not find an association of factor V Leiden mutation with venous thrombosis. In our VTE population, we found a significantly lower prevalence of hereditary thrombophilia among patients with cancer. After adjusting for other risk factors, thrombophilia was not found to be associated with cancer in our study.

In our cohort of VTE patients, PE and venous thrombosis of unusual sites including abdomen, superior and inferior vena cava and neck were more common in VTE patients with cancer than patients without cancer. These findings may have implications for clinical practice but warrant confirmation and further study. In our study, catheter-associated VTE was more common among patients with cancer but difference in catheter-associated thrombosis of the neck was not statistically significant between patients with and without cancer. There was also no significant difference in catheter-associated thrombosis between the two groups in the presence of thrombophilia. In contrast to these findings, a meta-analysis of ten studies involving 1,000 cancer patients suggested an association of central venous catheter-related thrombosis in the presence of factor V Leiden and prothrombin gene

mutations [42]. Another study by Tesselaar et al. [43] also reported an association of catheter-related thrombosis with elevated homocysteine levels in cancer patients.

Our multicenter study has a racial distribution similar to the general US population. Although not statistically significant, we found higher frequencies of race defined as “other” (non-white and non-black) and Hispanic ethnicity among patients with cancer. There were also racial and ethnic differences by sex, with black race among males and “other” race and Hispanic ethnicity among females more common among patients with cancer. As the prevalence of VTE is often reported by race and ethnicity [26,27], further studies may be needed to compare the characteristics and risk factors of cancer-associated VTE by race and ethnicity.

There are certain limitations in our study. As a patient registry conducted at Thrombosis and Hemostasis centers, there is a potential for referral bias in our study. Our cohort of VTE patients may be over representative of more complicated and recurrent cases of VTE compared to VTE cases treated elsewhere. In addition our cohort of patients with cancer may not be representative of all patients with cancer who develop VTE. The extent of malignancy with type and stage of cancer, histological grade and metastatic disease has been demonstrated to be important predictor for the risk of VTE in cancer patients as reported by several studies [5,36,44] but our data did not provide information about metastatic disease or stage and grade of cancer. We also could not evaluate the differences in risk factors by type and site of cancer due to our study design. In our study, we did not have information about the use of drugs other than chemotherapeutic agents, such as the use of erythropoiesis stimulating or antiangiogenic agents potentially affecting the thrombotic risk in these patients.

Venous thromboembolism (VTE) is a leading cause of morbidity and mortality in cancer patients and a complication of cancer treatment [3,6, 20,33,44,45]. However, the cross sectional design of our study did not permit us to evaluate differences in morbidity and mortality in our cohort of VTE patients. Large prospective studies with follow up data are needed to identify the characteristics of patients with cancer at a greater risk of developing incident and recurrent events of venous thromboembolism, major bleeding episodes and VTE related deaths.

This multi-site study demonstrates that VTE triggers may be different for those with cancer compared to those without cancer. In the absence of evidence based recommendations for thromboprophylaxis for cancer patients in outpatient settings [46], further studies are needed to identify cancer patients at higher risk of venous thromboembolism that could help reduce the thrombosis-associated morbidity and mortality in this population.

Acknowledgments

This work was supported by grants from the Centers for Disease Control and Prevention (DD000017 to CP, DD000235 to JAH, DD000016 to MMJ, DD000292 to SM, DD000014 to TLO, and DD000015 to the Hemophilia Foundation of Michigan [PLB, RK]).

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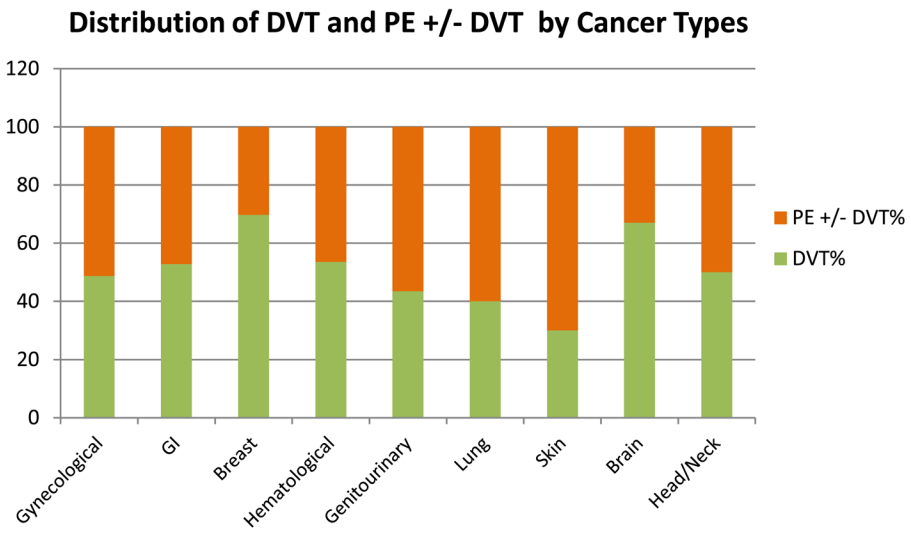

Fig. 1.
Distribution of DVT and PE+/− DVT by Cancer Types.

Table 1

Characteristics of VTE Patients with and without Cancer[a] at the time of enrollment.

Characteristics	VTE with Cancer (N = 189)	VTE without Cancer (N = 2,806)	p-value
Mean Age ± SD (years)[a]	57.1 ± 14.7	46.1 ± 15.5	<.0001
Median Age(years)[a]	57.9	45.4	<.0001
Mean age at first VTE ± SD (years)	52.2 ± 16.5	41.1 ± 15.7	<.0001
Median age at first VTE (years)	54.4	39.7	<.0001
Mean BMI ± SD (kg/m^2)[a]	29.2 ± 7.5	30.4 ± 7.9	0.05
	N (%)	N (%)	
Age group			
<45	31(16.4)	1,377(49.1)	<.0001
≥45	158(83.6)	1,429(50.9)	
Race[b]			
White	148(79.6)	2,247(80.9)	0.30
Black	30(16.1)	461(16.6)	
Others	8(4.3)	68(2.5)	
Hispanic	5(2.7)	69(2.5)	0.81
Sex			
Male	77(40.7)	1,060(37.8)	0.41
Female	112(59.3)	1,746(62.2)	
Smoking	11(5.8)	305(10.9)	0.03
BMI Categories(kg/m^2)[c]			
<18.5	5(2.9)	37(1.5)	0.06
18.5–25	52(30.2)	583(23.3)	
≥25	115(66.9)	1,880(75.2)	

[a] at the time of enrollment.

[b] race missing for 33 VTE patients (3 with cancer).

[c] bmi missing for 323 VTE patients (17 with cancer).

Table 2

Thrombophilia in VTE Patients with and without Cancer.

Thrombophilia	VTE with Cancer (N = 189) N (%)	VTE without Cancer (N = 2,806) N (%)	p-value
Thrombophilia	20(10.6)	703(25.1)	<0.001
Factor V Leiden	10(5.3)	337(12.0)	0.005
Prothrombin gene mutation	5(2.7)	86(3.1)	0.75
Protein C deficiency	0	39(1.4)	0.17
Protein S deficiency	3(1.6)	88(3.1)	0.23
Antithrombin III deficiency	0	21(0.7)	0.63
Antiphospholipid syndrome	4(2.1)	214(7.6)	0.005

Table 3

Distribution of VTE in Patients with and without Cancer.

	VTE with Cancer (N = 189)	VTE without Cancer (N = 2,806)	
	N (%)	N (%)	p-value
PE (+/− DVT)	92(48.7)	1,219(43.4)	0.16
DVT (No PE)	97(51.3)	1,587(56.6)	0.16
Arm	25(13.2)	263(9.4)	0.08
Leg	122(64.6)	1,828(65.2)	0.87
Superior Vena Cava	4(2.1)	11(0.4)	0.01
Inferior Vena Cava	6(3.2)	35(1.3)	0.04
Abdomen	11(5.8)	198(7.1)	0.52
Brain	0	79(2.8)	0.009
Neck	9(4.8)	46(1.6)	0.007
Catheter-associated VTE	9(4.8)	54(1.9)	0.02

Table 4

Types of Cancer in VTE Patients (N = 189).

Types of Cancer	N (%)
Gynecological	39(20.6)
Gastrointestinal	36(19.1)
Breast	33(17.5)
Hematological	28(14.8)
Genitourinary	23(12.2)
Lung	20(10.6)
Skin	10(5.3)
Brain	6(3.2)
Sarcoma	5(2.7)
Head and Neck	4(2.1)
VTE associated with	
Active Chemotherapy	41(21.7)
Active Radiotherapy	6(3.2)

Table 5

Unadjusted and Adjusted for Odds Ratios for Common VTE Risk Factors in VTE Patients with Cancer Compared to those without Cancer.

Characteristics	Unadjusted OR(95% CI)	Adjusted OR(95% CI)[c]
Age group ≥ 45 years	4.91(3.32,7.27)	5.20(3.30,8.18)
Male sex	1.13(0.84,1.53)	0.94(0.67,1.32)
Race[a]		
Blacks	0.99(0.66,1.48)	0.99(0.63,1.56)
Others	1.79(0.84,3.79)	1.65(0.71,3.84)
Hispanic	1.08(0.43,2.71)	1.21(0.42,3.52)
Smoking	0.48(0.25,0.91)	0.56(0.29,1.09)
BMI Categories[b]		
<18.5	1.52(0.57,4.02)	1.68(0.59,4.75)
≥25	0.69(0.49,0.96)	0.51(0.36,0.74)
Thrombophilia	0.35(0.22,0.57)	0.40(0.24,0.66)
Surgery	1.69(1.11,2.57)	1.86(1.19,2.91)
Hypertension	2.55(1.87,3.47)	1.66(1.15,2.40)
Hyperlipidemia	1.53(1.03,2.28)	0.96(0.61,1.51)

[a] White as ref group.

[b] BMI 18.5–25 kg/m^2 as ref group.

[c] Adjusted for all listed variables.

Table 6

Unadjusted and Adjusted for Odds Ratios for Common VTE Risk Factors in VTE Patients with Cancer Compared to Those without Cancer Stratified by Sex.

	Females		Males	
Characteristics	**Unadjusted OR (95% CI)**	**Adjusted OR (95% CI)[c]**	**Unadjusted OR (95% CI)**	**Adjusted OR (95% CI)[c]**
Age group ≥ 45 yrs	6.59(4.0,10.9)	5.79(3.2,10.5)	2.97(1.6,5.6)	3.27(1.6,6.7)
Race[a]				
Blacks	0.82(0.5,1.4)	0.69(0.4,1.3)	1.39(0.7,2.6)	1.65(0.8,3.3)
Others	2.16(0.9,5.2)	2.07(0.7,6.0)	1.19(0.3,5.2)	1.04(0.2,5.0)
Hispanic	1.28(0.5,3.6)	1.58(0.5,5.5)	0.69(0.1,5.2)	0.70(0.1,5.9)
BMI Categories[b]				
<18.5	1.43(0.4–4.9)	1.13(0.3–4.4)	1.58(0.3,7.8)	2.31(0.4,12.9)
BMI ≥25	0.77(0.5–1.2)	0.62(0.4–1.0)	0.49(0.3,0.9)	0.39(0.2,0.7)
Smoking	0.45(0.2,1.2)	0.57(0.2,1.5)	0.49(0.2,1.2)	0.46(0.2,1.2)
Surgery	1.4 (0.8, 2.5)		2.11(1.1,3.9)	2.55(1.3,4.9)
Hypertension	3.73(2.5,5.5)	2.15(1.3,3.5)	1.4 (0.8, 2.4)	
Hyperlipidemia	1.70(1.0,2.9)	0.82(0.4,1.5)	1.3 (0.7, 2.4)	
Diabetes	1.93(1.1,3.6)	0.92(0.4,1.9)	0.8 (0.3, 1.9)	
Thrombophilia	0.42(0.2,0.7)	0.45(0.2,0.8)	0.25(0.1,0.6)	0.29(0.1,0.8)
HRT	3.46(1.5,8.0)	2.33(0.9,5.8)		
OCP use	0.20(0.1,0.6)	0.35(0.1,1.7)		

[a] White as ref group.

[b] BMI 18.5–25 kg/m^2 as ref group.

[c] Adjusted for all listed variables.